

Amendments to the Claims:

The listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

Claims 1-26 (cancelled)

27. (new) A compound that inhibits PTP-1B and that interacts with at least one of the PTP-1B exosite-forming residues, wherein the compound includes a cyclic moiety and the compound is capable of forming a hydrogen bond, a salt bridge, or a van der Waals contact with at least one of the exosite-forming residues.
28. (new) The compound of claim 27 wherein the cyclic moiety is an aryl group.
29. (new) The compound of claim 27 wherein the cyclic moiety is a heteroaryl group.
30. (new) The compound of claim 27 wherein the exosite-forming residues are selected from the group consisting of Glu-186; Ser-187; Pro-188; Ala-189; Leu-192; Asn-193; Phe-196; Lys-197; Arg-199; Glu-200; Leu-272; Glu-276; Gly-277; Lys-279; Phe-280; Ile-281; and Met-282.
31. (new) The compound of claim 27 wherein the interaction is an amide-carbonyl, amide - hydroxyl, or amide - imidazole hydrogen bond, and the distance between the donor and acceptor atoms is between about 2.7 Angstroms and 3.3 Angstroms, or is a hydroxyl-hydroxyl or hydroxyl-carbonyl hydrogen bond, and the distance between the donor and acceptor atoms is between about 2.5 Angstroms and about 3.0 Angstroms.

32. (new) The compound of claim 27 wherein the interaction is a salt bridge that forms between an amino group and a carboxylic acid group, and the distance between the amino and carboxylic acid groups is about 2.5 Angstroms to about 4.0 Angstroms.

33. (new) The compound of claim 27 wherein the interaction is a van der Waals contact and is between a carbon or heteroatom in the compound and a carbon or a heteroatom in an exosite-forming residue and the distance between the carbon or heteroatom in the compound and a carbon or heteroatom in the residue is between about 2.0 Angstroms to about 5.0 Angstroms.

34. (new) The compound of claim 33 wherein the distance of the atoms participating in the van der Waals contact is between about 2.5 and about 3.5 Angstroms.

35. (new) The compound of claim 27 which is an isolated compound that is at least 99% pure as measured by weight.

36. (new) The compound of claim 27 wherein the compound does not comprise a polypeptide or an amino acid residue.

37. (new) A compound that inhibits TC-PTP and that interacts with at least one of the TC-PTP exosite-forming residues, wherein the compound includes a cyclic moiety and the compound is capable of forming a hydrogen bond, a salt bridge, or a van der Waals contact with at least one of the exosite-forming residues.

38. (new) The compound of claim 37 wherein the cyclic moiety is an aryl group.

39. (new) The compound of claim 37 wherein the cyclic moiety is a heteroaryl group.

40. (new) The compound of claim 37 wherein the exosite-forming residues are selected from the group consisting of Glu-186; Ser-187; Pro-188; Ala-189; Leu-192; Asn-193; Phe-196;

Lys-197; Arg-199; Glu-200; Met-272; Glu-276; Gly-277; Lys-279; Cys-280; Ile-281; and Lys-282 of TC-PTP.

41. (new) The compound of claim 37 wherein the interaction is an amide-carbonyl, amide hydroxyl, or amide imidazole hydrogen bond, and the distance between the donor and acceptor atoms is about 2.7 Angstroms and 3.3 Angstroms, or is a hydroxyl-hydroxyl or hydroxyl-carbonyl hydrogen bond, and the distance between the donor and acceptor atoms is between about 2.5 Angstroms and about 3.0 Angstroms.

42. (new) The compound of claim 37 wherein the interaction is a salt bridge between an amino group and a carboxylic acid group, and the distance between the amino and carboxylic acid groups is about 2.5 Angstroms to about 4.0 Angstroms.

43. (new) The compound of claim 37 wherein the interaction is a van der Waals contact between a carbon or heteroatom in the compound and a carbon or a heteroatom in an exosite-forming residue and the distance between the carbon or heteroatom in the compound and a carbon or heteroatom in the residue is between about 2.0 Angstroms to about 5.0 Angstroms.

44. (new) The compound of claim 43 wherein the distance of the atoms participating in the van der Waals contact is between about 2.5 and about 3.5 Angstroms.

45. (new) The compound of claim 37 which is an isolated compound that is at least 99% pure as measured by weight.

46. (new) The compound of claim 37 wherein the compound does not comprise a polypeptide or an amino acid residue.

47. (new) A method of identifying an exosite inhibitor of PTP-1B comprising:
a) contacting the exosite of PTP-1B with a test compound; and
b) determining the activity of PTP-1B.

48. (new) The method of claim 47 wherein the activity of PTP-1B is the removal of a phosphate group on a substrate upon binding to the active site of PTP-1B.

49. (new) A method of identifying an exosite inhibitor of PTP-1B comprising:

a) contacting a test compound with PTP-1B having one or more amino acid residues selected from the group consisting of Glu-186; Ser-187; Pro-188; Ala-189; Leu-192; Asn-193; Phe-196; Lys-197; Arg-199; Glu-200; Leu-272; Glu-276; Gly-277; Lys-279; Phe-280; Ile-281; and Met-282; and

b) determining the activity of PTP-1B.

50. (new) The method of claim 49 further comprising the step of identifying the exosite inhibitor of PTP-1B by comparing the activity of PTP-1B in the presence of the test compound with the activity of the exosite mutant of PTP-1B in the presence of the test compound.

51. (new) The method of claim 50 further comprising the step of preparing a pharmaceutical composition by admixing the inhibitor compound identified with at least one pharmaceutically acceptable excipient.

52. (new) The method of claim 49 wherein the exosite inhibitor is an organic polycyclic aromatic compound.

53. (new) The method of claim 49 wherein the residue is selected from the group consisting of Asn-193, Phe-196, Lys-197, Arg-199; Glu-276, and Phe-280.

54. (new) The method of claim 49 wherein the residues are Asn-193 and Phe-196.

55. (new) The method of claim 49 wherein the residues are Asn-193 and Phe-280.

56. (new) A method of identifying an exosite inhibitor of TC-PTP comprising:

- a) contacting the exosite of TC-PTP with a test compound; and
- b) determining the activity of TC-PTP.

57. (new) The method of claim 56 wherein the activity of TC-PTP is the removal of a phosphate group on a substrate upon binding to the active site of TC-PTP.

58. (new) A method of identifying an exosite inhibitor of TC-PTP comprising

- a) contacting a test compound with TC-PTP having one or more amino acid residues selected from the group consisting of Glu-186; Ser-187; Pro-188; Ala-189; Leu-192; Asn-193; Phe-196; Lys-197; Arg-199; Glu-200; Met-272; Glu-276; Gly-277; Lys-279; Cys-280; Ile-281; and Lys-282 of TC-PTP; and
- b) determining the activity of TC-PTP.

59. (new) The method of claim 58 further comprising the step of identifying the exosite inhibitor of PTP-1B by comparing the activity of TC-PTP in the presence of the test compound with the activity of the exosite mutant of TC-PTP in the presence of the test compound.

60. (new) The method of claim 59 further comprising the step of preparing a pharmaceutical composition by admixing the inhibitor compound identified with at least one pharmaceutically acceptable excipient.

61. (new) The method of claim 59 wherein the exosite inhibitor is an organic polycyclic aromatic compound.

62. (new) The method of claim 58 wherein the residue is selected from the group consisting of Asn-193; Phe-196; Lys-197; Arg-199; Glu-276; and Cys-280.

63. (new) The method of claim 58 wherein the residues are Asn-193 and Phe-196.

64. (new) The method of claim 58 wherein the residues are Asn-193 and Cys-280.